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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/758,799	01/11/2001	Thomas R. Porter	P00639US3	1046

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EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/758,799	PORTER, THOMAS R.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Nov 04, 2003, Dec 19, 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53-69 and 71-78* is/are pending in the application.

4a) Of the above claim(s) *53-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-69 and 71-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 04, 2003 has been entered.

New matter rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 66-69, 71-78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the instant case, the recitation of "distal to the thrombus site" in claim 66 was not disclosed in neither the specification of the instant application nor the originally presented claims. Although the specification described the use of microbubbles to relieve thrombus obstruction, there is no specific teaching about relieving trauma associated with the obstruction of vessels distal to the thrombus site. Thus, the claims are rejected as it incorporates new matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 66-69, 71, 75-78 are rejected under 35 U.S.C. 102(b) as being anticipated by Tachibana et al US Patent 5,315,998 or Feinstein US Patent 4,718,433.

The instant claims are directed to methods of relieving trauma comprising introducing a pharmaceutical composition to an animal with a thrombus by intravenous injection, said composition comprising microbubble and a carrier wherein said carrier comprises 5% solution dextrose and applying ultrasound to the area of trauma, distal to the thrombus.

Applicant is first informed that in process claims, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Both Tachibana and Feinstein teach all elemental process steps of the instant claims thus, they anticipate the limitations of the instant claims.

Tachibana discloses methods of administering to a subject with thrombosis microbubble compositions in a liquid 3 to 5% human serum albumin solution in dextrose and applying ultrasound energy to the region of interest to enhance thrombolysis. (see abstract, col 4, lines 20-65; col 6, lines 15-col 8, line 5). Tachibana discloses method steps that are the same as those instantly claimed. There is no manipulative difference

between Tachibana's method and those instantly claimed. Therefore, Tachibana inherently meets the limitations of the instant claims.

Feinstein teaches methods of administering a composition comprising microbubble in 5% solution of albumin in dextrose and further conducting ultrasound imaging from the site of interest including myocardial tisses that are subject to a trauma such as coronay artery angioplasty, clotted coronary arteries, etc.. (see abstract, col 7, lines 55-col 8, line 10). There is no manipulative difference between Feinstein's method and those instantly claimed. Therefore, Feinstein inherently meets the limitations of the instant claims.

Also, the pending claims on their face do not require "thrombus dissolution and recanalization." Note that the claim states "with or without thrombus dissolution and recanalization." Therefore, Tachibana's and Feinstein's mere application of ultrasound energy to the traumatized region meets the intended use of the instant claims.

Further, Applicant is reminded that during examination of a patent application the words of a claim are given their "plain meaning" unless they are defined in the specification. see MPEP 2111.01. Absence of clear definition in the specification, the claims must be interpreted as broadly as their terms reasonably allow. Therefore, during patent examination the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. *Id.*

In the instant case, the specification does not provide clear definition of to what "distal to the thrombus site" exactly refers? The region that the ultrasound waves is radiating or the region from which the source of ultrasound waves is located.

Accordingly, at least one interpretation of the instant limitation is directed to the location of the ultrasound source. Since, both Tachibana and Feinstein radiate their ultrasound waves ex vivo and/ or distally from the surface of the body, they meet the instant limitation of "distal to the thrombus site."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 66-69, 71-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siegel in view of Tachibana et al US Patent 5,315,998, Feinstein US Patent 4,718,433 and further in view of Schutt US Patent 5,605,673 (Schutt).

Siegel discloses methods of for utilizing a combination of ultrasonic energy and an echo contrast agent containing microbubbles for dissolving blood clots or other vascular obstructions (see abstract). Siegel specifically discloses the use of echo contrast agents containing dodecafluoropentane and sonicated albumin (see col 2, lines

48-57). Siegel further discloses the use of a thrombolytic agent in combination to the contrast agents mentioned above (see col 3, lines 14-40, col 9-14, claims 1, 10, 15). Finally, Siegel discloses the use of Albunex as the suitable sonicated albumin. Albunex contain microbubbles having average diameter size within 2-10 micron (see de Jong abstract, Ultrasonic 1993; 31(3):175-181). Siegel fails to specifically disclose the optimal concentrations for the albumin and a Dextrose carrier.

Tachibana and Feinstein collectively set forth various suitable concentrations and methodologies for employing albumin and a dextrose carrier system. Tachibana 5% dextrose in combination with streptokinase (see col 6, line 15-col 8, line 5). Feinstein teaches methods of formulating Albunex echo contrast agent and applying it to a traumatized coronary tissue. (see abstract, col 5, line 45-col 6, line 40; col 8, lines 1-49). col 2, lines 46-68, col 8, lines 1-46). Feinstein also acknowledge the use of their contrast agents in treating blood flow abnormalities (see col 8, lines 1-10). However, Tachibana and Feinstein do not employ perfluorinated gases in their microbubble containing contrast agents in treating thrombus associated blood flow abnormalities.

Schutt provides for the use of various types of perfluorinated gases such as perfluorobutane and perfluoropropane in protein-shelled gaseous microbubbles in ultrasound contrast agents. (see abstract, col 16, lines 1-30). Schutt also suggests the use of his pefluorocarbon containing microbubbles in enhancing coronary flow with thrombolytic agents (col 11, lines 28-33).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize the concentrations of albumin and dextrose in the Siegel's

formulations, as suggested in Tachibana and Feinstein and Cerny, by routine experimentation, and further substitute the decafluorpentane of Siegel with other perfluorocarbons such as perfluorbutane or perfluoropropane, because as shown by Schutt, such moieties are considered to be art equivalent, and absence of showing unexpected results, they are expected to provide similar therapeutic results.

Response to Arguments

Applicant's arguments with respect to claims 66-69, 71-78 have been considered but are moot in view of the new ground(s) of rejection. Nevertheless, Examiner addresses a few issues that may be applicable to the new grounds.

Applicant argues that Siegel discloses not teach or suggest any method for relieving trauma associated with obstruction of vessels distal to a thrombus site by increasing blood flow with or without thrombus dissolution and recanalization in animals. (see page 8, 3rd para. of the arguments). In response Examiner first states that Applicant's arguments amount to a mere distinguish in the intended use of Siegel's methods. Such arguments alone without any manipulative difference in process steps do not amount to a patentable subject matter as reasoned above.

Further, the claim on its face does not require "thrombus dissolution and recanalization." Note that the claim states with or without thrombus dissolution and recanalization. Therefore, Siegel's mere application of ultrasound energy to any region meets this limitation.

Finally, even though Siegel may not explicitly recited "relieving trauma associated with obstruction of vessels distal to a thrombus site." Achievement of such result is

inevitable outcome of Siegel's method because once the obstruction is dissolved; patient would be relieved of the trauma associated with such obstruction.

Applicant also asserted that unlike the instant claims, both Feinstein and Schutt teach administration of a thrombolytic agent to dissolve the clot (see page 9, 2nd para.). This argument, however, is not commensurate with the scope of the claims, because the instant claims uses do not exclude the use of such agents as they use "comprising" as the transitional phrase.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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RUSSELL TRAVERS
PRIMARY EXAMINER